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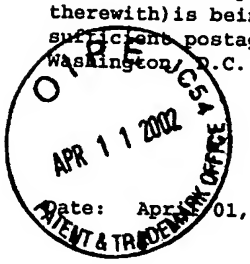

Date: April 01, 2002

John P. Parise
(Print Name)

(Signature)

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Group No.: 1743

Manfred Kansy, et al.

Serial No.: 10/077,363

Filed: February 15, 2002

For: **CUVETTE ARRAYS**

TRANSMITTAL OF CERTIFIED COPY

April 01, 2002

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Attached please find the certified copy of the foreign application from which priority is claimed for this case:

Country	Application No.	Filing Date
Europe	01810178.2	February 20, 2001

Respectfully submitted,

John P. Parise
Attorney for Applicant
Reg. No. 34403
Hoffmann-La Roche Inc.
340 Kingsland Street
Nutley, New Jersey 07110
Phone: (973) 235-6326

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Bescheinigung | Certificate | Attestation

Die angehefteten Unterlagen stimmen mit der ursprünglich eingereichten Fassung der auf dem nächsten Blatt bezeichneten europäischen Patentanmeldung überein.

The attached documents are exact copies of the European patent application described on the following page, as originally filed.

Les documents fixés à cette attestation sont conformes à la version initialement déposée de la demande de brevet européen spécifiée à la page suivante.

Patentanmeldung Nr. Patent application No. Demande de brevet n°

01810178.2

Der Präsident des Europäischen Patentamts;
Im Auftrag

For the President of the European Patent Office

Le Président de l'Office européen des brevets
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Blatt 2 der Bescheinigung
Sheet 2 of the certificate
Page 2 de l'attestation

Anmeldung Nr.:
Application no.: 01810178.2
Demande n°:

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Date of filing: 20/02/01
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Anmelder:
Applicant(s):
Demandeur(s):
F. HOFFMANN-LA ROCHE AG
4070 Basel
SWITZERLAND
Weidmann Plastics Technology AG
8640 Rapperswil
SWITZERLAND

Bezeichnung der Erfindung:
Title of the invention:
Titre de l'invention:

Linear cuvette array, a two-dimensional cuvette array built therewith and a system comprising such two-dimensional cuvette arrays

In Anspruch genommene Priorität(en) / Priority(ies) claimed / Priorité(s) revendiquée(s)

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LINEAR CUVETTE ARRAY, A TWO-DIMENSIONAL CUVETTE ARRAY BUILT THEREWITH AND A SYSTEM COMPRISING SUCH TWO-DIMENSIONAL CUVETTE ARRAYS

The invention concerns an integrally built, linear array of cuvettes made of a plastic material, every cuvette of the array having the same shape and dimensions, and neighboring cuvettes being connected to each other by a single web.

The invention also concerns a two-dimensional array of cuvettes.

The invention also concerns a system comprising two or more two-dimensional arrays of cuvettes.

In the field of chemical analysis of samples, differential expression analysis (profiling) of genes and gene fragments and in particular in the field of screening of pharmaceutical compounds and in bio-diagnostics of such compounds and samples large numbers of such compounds should be analyzed as fast as possible. There is therefore a need for a system of cuvette arrays making it possible to perform diffusion or filtration process steps as well as analytical measurements simultaneously or sequentially on a plurality of liquid samples in order to perform a high throughput screening of those samples.

A first aim of the invention is therefore to provide a linear array of cuvettes which is apt to be used as a basic component of such a system.

A second aim of the invention is to provide a two-dimensional array of cuvettes which is apt to be used as a component of such a system.

A third aim of the invention is to provide a system of cuvette arrays which allows to perform diffusion or

filtration process steps as well as analytical measurements simultaneously or sequentially on a plurality of samples and in an optimum way in order to achieve the desired high throughput screening of those samples in an optimum way.

According to the invention the first aim mentioned above is attained with a linear array according to claim 1.

According to the invention the second aim mentioned above is attained with a two-dimensional array of cuvettes according to claim 3.

According to the invention the third aim mentioned above is attained with a system according to claim 13 for simultaneously performing diffusion or filtration process steps as well as analytical measurements simultaneously or sequentially on a plurality of liquid samples.

The main advantages of the invention are that it allows to perform the desired process steps efficiently and with great flexibility, at a relatively low cost, and at the same time makes it possible to overcome problems encountered with prior art devices.

Preferred embodiments of the invention are described hereinafter with reference to the accompanying drawings wherein

Fig. 1 shows a top view of a linear cuvette array 11 according to the invention,

Fig. 2 shows a cross-section through a plane A-A of linear cuvette array 11 in Fig. 1,

Fig. 3 shows a cross-sectional view of one of the cuvettes 12 of linear cuvette array 11 in Fig. 1,

Fig. 4 shows a cross-sectional view of one of the cuvettes 12 of linear cuvette array 11 in Fig. 1, this cuvette including a foil shaped layer 61 attached to the lower end of the cuvette,

Fig. 5 shows a top view of a cuvette holder 32 forming part of a two-dimensional cuvette array according to the invention,

Fig. 6 shows a cross-section through a plane B-B of cuvette holder 32 in Fig. 5,

Fig. 7 shows a top view of a two-dimensional cuvette array 31 according to the invention,

Fig. 8 shows a cross-section through a plane C-C of two-dimensional cuvette array 31 in Fig. 7,

Fig. 9 shows a cross-sectional representation of stacked two-dimensional cuvette arrays 31 and 41,

Fig. 10 shows a cross-sectional representation of a two-dimensional cuvette array 31 stacked onto a standard analysis multiwell plate 38.

Figures 1 and 2 show an integrally built, linear array 11 of cuvettes 12, 13, 14, etc. made of a plastic material.

Every cuvette of array 11 has the same shape and dimensions and neighboring cuvettes are connected to each other by a single web 15, 16. Each of these single webs 15, 16 has a curved shape.

The symmetry axis Y-Y of every cuvette 12 which forms part of array 11 of cuvettes lies substantially in one and the same plane A-A which is a symmetry plane of cuvette array

11. The upper part of an intermediate cuvette 12 of array 11 is connected by a first single web 15 to a neighboring cuvette 13 which lies on one side of intermediate cuvette 12 and is connected by a second single web 16 to a neighboring cuvette 14 which lies on the opposite side of intermediate cuvette 12. First single web 15 and second single web 16 lie on opposite sides of said symmetry plane A-A.

Webs 15, 16 are flexible and therefore facilitate the insertion of the cuvettes in a cuvette holder, e.g. cuvette holder 32 described hereinafter, in spite of variations of the length of cuvette array 11 which are due to different shrinkage coefficients of the different materials used for manufacture of cuvette arrays 11 by injection molding.

Each one of cuvettes 2 and 7 (this numbers indicate the relative position of the cuvettes of the array) of cuvette array 11 has three radially oriented ribs 19, 29 which serve for accurately positioning the cuvette into an opening of cuvette holder 32 described hereinafter.

Each one of cuvettes 1, 3, 6, 8 or 1, 3-6, 8 (this numbers indicate the relative position of the cuvettes of the array) of cuvette array 11 has e.g. latches 21 and 22 which are an integral part of the cuvette and which serve for removably connecting the cuvette to cuvette holder 32 described hereinafter.

Fig. 2 shows a cross-section of one of the cuvettes, e.g. cuvette 12, of cuvette array 11. As shown by Fig. 2, the cuvette has an upper chamber 17 and a lower chamber 18 which have a common symmetry axis Y-Y which passes through the centers of both chambers. Upper chamber 17 and lower chamber 18 have each a substantially cylindrical shape. The cross-section of upper chamber 17 at the central part thereof is larger than the cross-section of lower chamber 18.

Lower chamber 18 has an open lower end 23. Upper chamber 17 has an open top end 24 and an annular bottom wall 25. This bottom wall has a central circular opening 26 which connects said upper chamber 17 with lower chamber 18.

The inner surface 27 of bottom wall 25 is part of a conical surface the cross-section of which forms an angle of about 80 degrees with the symmetry axis Y-Y of the cuvette, so that there is an abrupt change of cross-section between said upper chamber 17 and said lower chamber 18.

The cuvette array 11 is made by injection molding of a selected first plastic material which is particularly suitable for being used in combination with a second selected material of which a foil shaped layer is made. This layer is adapted to be closely attached to each cuvette of the array of cuvettes for covering at least one opening of each cuvette.

The attachment of the foil shaped layer to each cuvette can be effected e.g. by gluing the layer and the cuvette or by a welding process. The foil attached to each individual cuvette is attached only to this individual cuvette and has no connection with any other cuvette or with a foil attached to a different cuvette.

The attachment of the layer to the cuvette must ensure a medium tight connection (liquid and/or gas tight connection) of these components.

Possible uses of such a foil shaped layer include e.g. its use as a filter and/or as a transparent closure (e.g. transparent to ultraviolet irradiation), which must not necessarily have the function of a filter.

When the foil shaped layer is used as a filter, the filtration process can be effected by use of vacuum or pressure applied to the medium contained in each cuvette of a cuvette array.

Suitable materials for a foil shaped layer usable as a filter and having a thickness in a range of 10 to 200 micrometer are for instance:
polyvinylidenfluorid (PVDF), polycarbonat (PC), polysulfon (PSU), regenerated cellulose, polytetrafluorethylen (PTFE), PET, and filter paper.

As shown by Figure 4 such a foil shaped layer is adapted to be closely attached to the lower end of the cuvette. Fig. 4 shows a cuvette 12 and a foil shaped layer 61 which is closely attached to cuvette 12 for covering the opening of this cuvette at the lower end 23 thereof.

The injection molding apparatus for manufacturing the cuvette array is preferably so configured and dimensioned that injection molding of different materials having different shrinkage coefficients can be carried out with one and the same apparatus.

In order to obtain a high stability of the assembly formed by a cuvette array 11 and the above mentioned foil shaped layer, the material of which this layer is made is so selected that properties of the layer are suitable for use with the material of which the cuvettes are made.

On the other hand the materials of the cuvette array and of the foil shaped layer are so selected that they are particularly well adapted for and thereby enable optimization of a particular process carried out with the assembly of cuvette array and foil shaped layer. Such processes are e.g. filtration, diffusion, concentration determination, "microspotting".

For instance, cuvettes made of an hydrophilic material, e.g. celluloseacetate, are suitably combined with ultrafiltration membranes for carrying out ultrafiltrations in an optimal way. Diffusion processes through artificial membranes are preferably carried out with hydrophobic filtration membranes, which are suitable for being combined by a melting process with cuvette material having similar hydrophobic properties. Filtration processes require hydrophilic or lipophilic properties of the cuvettes and of the filtration membrane attached thereto, and the selection of the materials of these components depends from the properties of the substance to be filtered.

For processes involving genes or genes fragments are deposited by microspotting on the foil which is attached to the lower end of the cuvettes of cuvette array 11.

Following materials are examples of materials which can be used to manufacture cuvette array 11: celluloseacetate, polycarbonate, polyvinylidene fluoride (PVDF), polysulfones, polystyrene, polypropylene (PP). Materials with similar shrinkage coefficient (in connection with injection molding) and melting properties may also be used for manufacturing cuvette array 11.

Fig. 5 shows a top view of a cuvette holder 32 which can be used to hold a plurality of the above described cuvette arrays 11 to form a two-dimensional cuvette array 31. Fig. 6 shows a cross-section through a plane B-B of cuvette holder 32 in Fig. 5.

In a preferred embodiment cuvette holder 32 is of substantially rectangular shape and has four centering ribs located each on the outer surface of one of the corners of cuvette holder 32.

Fig. 7 shows a top view of a two-dimensional cuvette array 31 according to the invention. Fig. 8 shows a cross-section through a plane C-C of two-dimensional cuvette array 31 in Fig. 7.

As can be appreciated from Figures 7 and 8, a two-dimensional array 31 of cuvettes according to the invention comprises a cuvette holder 32 having a matrix array 33 of openings 34 for receiving cuvettes 12 of at least one linear cuvette array 11 having the above described features. Each of the cuvettes 12 of cuvette array 11 has a shape and dimensions that snugly fits into one of openings 34 of cuvette holder 32.

Cuvette holder 32 is so configured and dimensioned that two-dimensional array 31 is adapted to be used in a centrifugator. As shown by Fig. 8, cuvette holder 32 snugly fits into a holder plate 39 of a centrifugator.

As shown by Fig. 9, two or more two-dimensional cuvette arrays e.g. arrays 31 and 41 each of which has the structure described above with reference to Figures 7 and 8 can be stacked on each other to form a three-dimensional cuvette array. According to the invention, the components of such an array are so configured and dimensioned that cuvettes having the same relative position in their respective holders are accurately positioned one above the other with coincidence of their symmetry axis, one of said cuvettes taking the position of an upper cuvette 51 and the other cuvette taking the position of a lower cuvette 52. In a preferred embodiment a portion of the lower part of each upper cuvette 51 lies within the upper chamber of the corresponding lower cuvette 52 and the lower end of the upper cuvette 51 is at a predetermined distance from the bottom wall of the upper chamber of the lower cuvette 52.

As shown by Fig. 10, a two-dimensional cuvette array 31 which has the structure described above with reference to Figures 7 and 8 can be stacked also on a standard holder plate 38 for a standard multiwell plate.

According to the invention a system comprising one or more two-dimensional arrays 31, 41, etc. of cuvettes having the above-described structure are used to perform simultaneously diffusion, filtration or detection process steps on a plurality of liquid samples, wherein said samples are e.g. genes, gene fragments, drug substance or precursors of drugs.

In a preferred embodiment such a system comprises a first two-dimensional cuvette array 31 and a second two-dimensional cuvette array 41, said cuvette arrays 31, 41 are stacked on each other, and the cuvette holders 32, 42 and the cuvettes 12 of said two-dimensional cuvette arrays 31, 41 are so configured and dimensioned that cuvettes having the same relative position in their respective holders are accurately positioned one above the other with coincidence of their symmetry axis, one of the cuvettes taking the position of an upper cuvette 51 and the other cuvette taking the position of a lower cuvette 52. In a preferred embodiment a portion of the lower part of the upper cuvette 51 lies within the upper chamber of the lower cuvette 52 and the lower end of the upper cuvette 51 is at a predetermined distance from the bottom wall of the upper chamber of the lower cuvette 52. With this arrangement there is no capillary gap between liquid contained in the lower part of the upper cuvette 51 and liquid contained in the upper chamber of the lower cuvette 52.

List of reference numbers

11	linear cuvette array
12	cuvette
13	cuvette
14	cuvette
15	web
16	web
17	upper chamber
18	lower chamber
19	rib
21	latch
22	latch
23	open low end
24	open top end
25	bottom wall
26	opening
27	inner surface of bottom wall 25
28	
29	rib
31	two-dimensional cuvette array
32	cuvette holder
33	matrix array of openings
34	opening (for receiving cuvettes)
35	
36	
37	
38	standard holder plate for a standard multiwell plate
39	holder plate of a centrifugator
41	two-dimensional cuvette array
42	cuvette holder
43	holder plate
51	upper cuvette
52	lower cuvette
61	foil shaped layer

Modifications and alternative embodiments of the invention will be apparent to those skilled in the art in view of the foregoing description. Accordingly, this description is to be construed as illustrative only and is for the purpose of teaching those skilled in the art the best mode of carrying out the invention. Details of the apparatus and of the system described may be varied without departing from the spirit of the invention and the exclusive use of all modifications which come within the scope of the appended claims is reserved.

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Claims

1. An integrally built, linear array of cuvettes made of a plastic material, every cuvette of the array having the same shape and dimensions, and neighboring cuvettes being connected to each other by a single web, said array of cuvettes being characterized in that

(a) each of said single webs (15, 16) has a curved shape,

(b) each cuvette (12) has means (19, 29) forming integral part thereof and serving for accurately positioning said cuvette (12) into an opening of a cuvette holder and means (21, 22) for removably connecting said cuvette (12) to said cuvette holder,

(c) each cuvette (12) has an upper chamber (17) and a lower chamber (18) having a common symmetry axis (Y-Y) passing through the centers of both chambers, each of said upper and lower chambers having a substantially cylindrical shape, and the cross-section of said upper chamber (17) at the central part thereof being larger than the cross-section of said lower chamber (18),

(d) said lower chamber (18) has an open lower end (23),

(e) said upper chamber (17) has an open top end (24) and an annular bottom wall (25) having a central circular opening (26) which connects said upper chamber (17) with said lower chamber (18), the inner surface (27) of said bottom wall (25) being part of a conical surface the cross-section of which forms an angle of about 80 degrees with the symmetry axis (Y-Y) of said cuvette (12), so that there is an abrupt change of cross-section between said upper chamber (17) and said lower chamber (18), and

(f) said array of cuvettes is made of a selected first plastic material which is particularly suitable for being used in combination with a second selected material of which a foil shaped layer (61) is made, said layer being adapted to be closely attached to each cuvette (12) of said array of

cuvettes for covering at least one opening of each cuvette (12).

2. The linear cuvette array according to claim 1, wherein the symmetry axis (Y-Y) of every cuvette (12) forming part of said array (11) of cuvettes lies substantially in one and the same plane (A-A) which is a symmetry plane of said cuvette array (11), the upper part of each intermediate cuvette (12) of the array is connected by a first single web (15) to a neighboring cuvette (13) lying on one side of said intermediate cuvette (12) and is connected by a second single web (16) to a neighboring cuvette (14) lying on the opposite side of said intermediate cuvette (12), said first and second single webs (15, 16) lying on opposite sides of said symmetry plane (A-A).

3. A two-dimensional array of cuvettes comprising

(a) a cuvette holder (32) having a matrix array (33) of openings (34) for receiving cuvettes (12), and

(b) at least one linear cuvette array (11) according to claim 1, each cuvette (12) of said at least one cuvette array (11) having a shape and dimensions that snugly fits into one of said openings (34) of said cuvette holder (32).

4. The two-dimensional array of cuvettes according to claim 3, wherein said cuvette holder (32) and the cuvettes (12) of said at least one linear cuvette array (11) are so configured and dimensioned that two or more cuvette holders (32) carrying each at least one linear cuvette array (11) can be stacked in such a way that cuvettes having the same relative position in their respective holders are accurately positioned one above the other with coincidence of their symmetry axis, one of said cuvettes taking the position of an upper cuvette (51) and the other cuvette taking the position of a lower cuvette (52), a portion of the lower part of the upper cuvette (51) lying within the upper chamber of the lower cuvette (52) and the lower end of the

upper cuvette (51) being at a predetermined distance from the bottom wall of the upper chamber of the lower cuvette (52).

5. The two-dimensional array of cuvettes according to claim 3 or 4, further comprising a foil (61) which is attached to the lower end of each cuvette (12) for covering the opening (23) of said cuvette at that lower end thereof.

6. The two-dimensional array of cuvettes according to claims 5, wherein said foil is a filter.

7. The two-dimensional array of cuvettes according to claims 5, wherein said foil is transparent.

8. The two-dimensional array of cuvettes according to claims 5, wherein said foil carries genes or gene fragments deposited on said foil by microspotting.

9. The two-dimensional array of cuvettes according to claim 3 or 4, wherein said cuvette holder (32) is of substantially rectangular shape and has four centering ribs located each on the outer surface of one of the corners of said cuvette holder (32).

10. The two-dimensional array of cuvettes according to claim 3 or 4, wherein said cuvette holder (32) is so configured and dimensioned that said two-dimensional array (31) of cuvettes is adapted to be used in a centrifugator.

11. A system for simultaneously performing diffusion or filtration process steps on a plurality of liquid samples, said system comprising one or more two-dimensional arrays of cuvettes according to any of claims 3 to 10.

12. The system according to claim 11 comprising a first two-dimensional cuvette array (31) according to claim 3 and

a second two-dimensional cuvette array (41) according to claim 3, wherein said cuvette arrays are stacked on each other, and wherein the cuvette holders (32, 42) and the cuvettes (12) of said two-dimensional cuvette arrays (31, 41) are so configured and dimensioned that said two-dimensional cuvette arrays (31, 41) can be stacked in such a way that cuvettes having the same relative position in their respective holders are accurately positioned one above the other with coincidence of their symmetry axis, one of said cuvettes taking the position of an upper cuvette (51) and the other cuvette taking the position of a lower cuvette (52), a portion of the lower part of the upper cuvette (51) lying within the upper chamber of the lower cuvette (52) and the lower end of the upper cuvette (51) being at a predetermined distance from the bottom wall of the upper chamber of the lower cuvette (52).

- - - - -

Abstract

An integrally built, linear array of cuvettes made of a plastic material, every cuvette of the array having the same shape and dimensions, and neighboring cuvettes being connected to each other by a single web. In the linear array of cuvettes each of said single webs (15, 16) has a curved shape, each cuvette (12) has means (19, 29) forming integral part thereof and serving for accurately positioning said cuvette (12) into an opening of a cuvette holder and means (21, 22) for removably connecting said cuvette (12) to said cuvette holder. Each cuvette (12) has an upper chamber (17) and a lower chamber (18) having a common symmetry axis (Y-Y) passing through the centers of both chambers. Each of the upper and lower chambers (17, 18) has a substantially cylindrical shape. The cross-section of said upper chamber (17) at the central part thereof is larger than the cross-section of the lower chamber (18). The lower chamber (18) has an open lower end (23). The upper chamber (17) has an open top end (24) and an annular bottom wall (25) having a central circular opening (26) which connects the upper chamber (17) with the lower chamber (18). The inner surface (27) of the bottom wall (25) of the upper chamber (17) is part of a conical surface the cross-section of which forms an angle of about 80 degrees with the symmetry axis (Y-Y) of the cuvette (12), so that there is an abrupt change of cross-section between the upper chamber (17) and the lower chamber (18). A two-dimensional array of cuvettes (31, 41) comprises a plurality of linear cuvette arrays (11) inserted into a cuvette holder (32, 42) having a matrix array of cuvette receiving openings (34). A system of two-dimensional cuvette arrays is built by stacking two or more of such two-dimensional arrays (31, 41) of cuvettes. Foil shaped layers serving, e.g. as a filter, are adapted to be attached to each cuvette to cover at least one opening thereof.

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(Fig. 1)

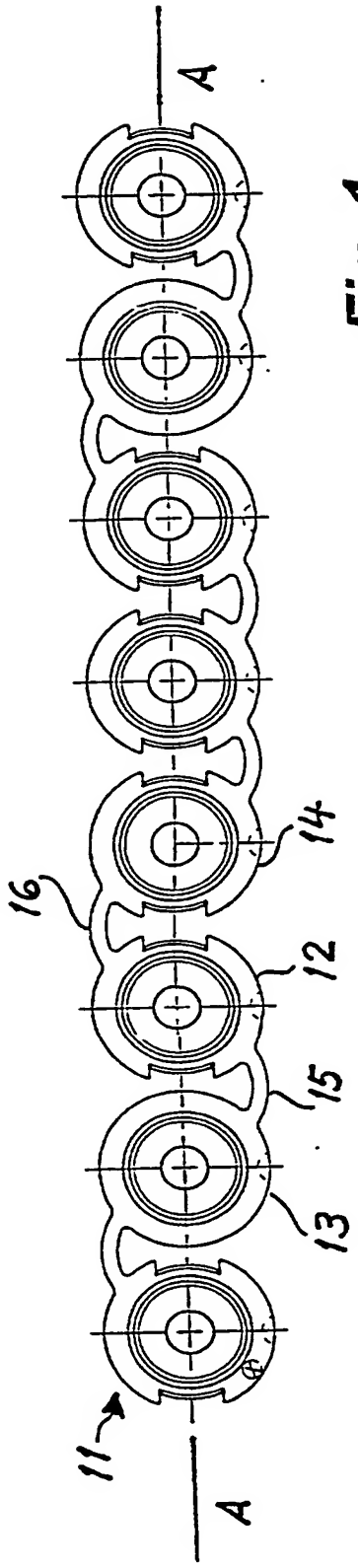


Fig. 1

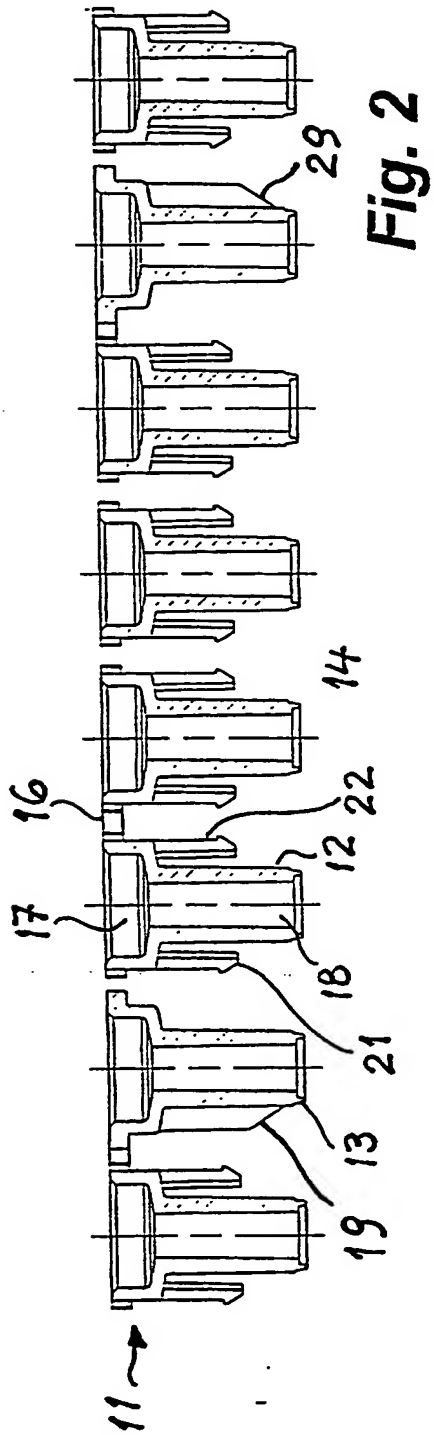


Fig. 2

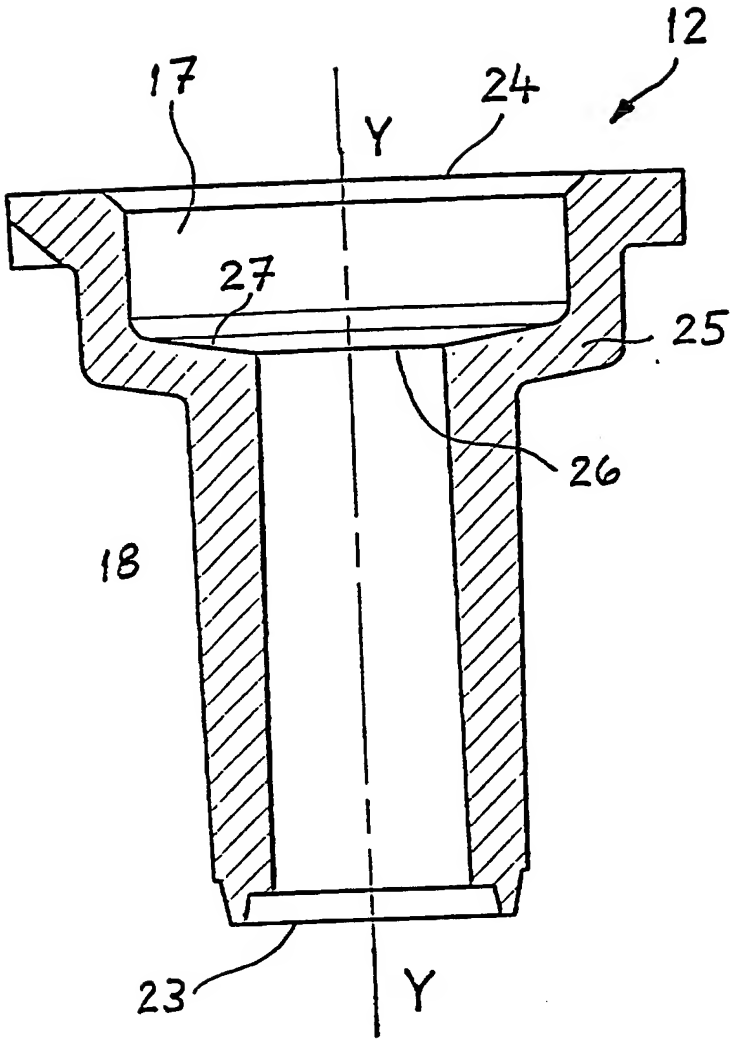


Fig. 3

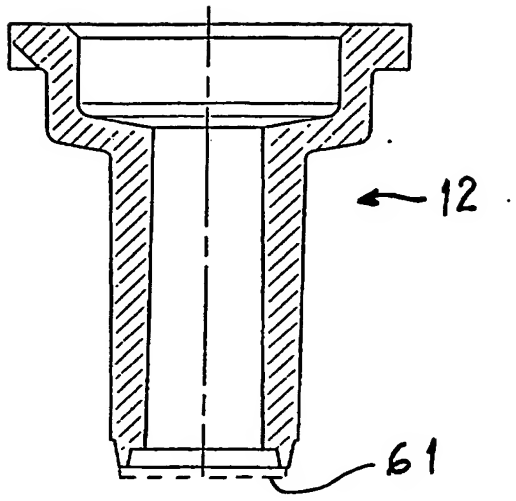


Fig. 4

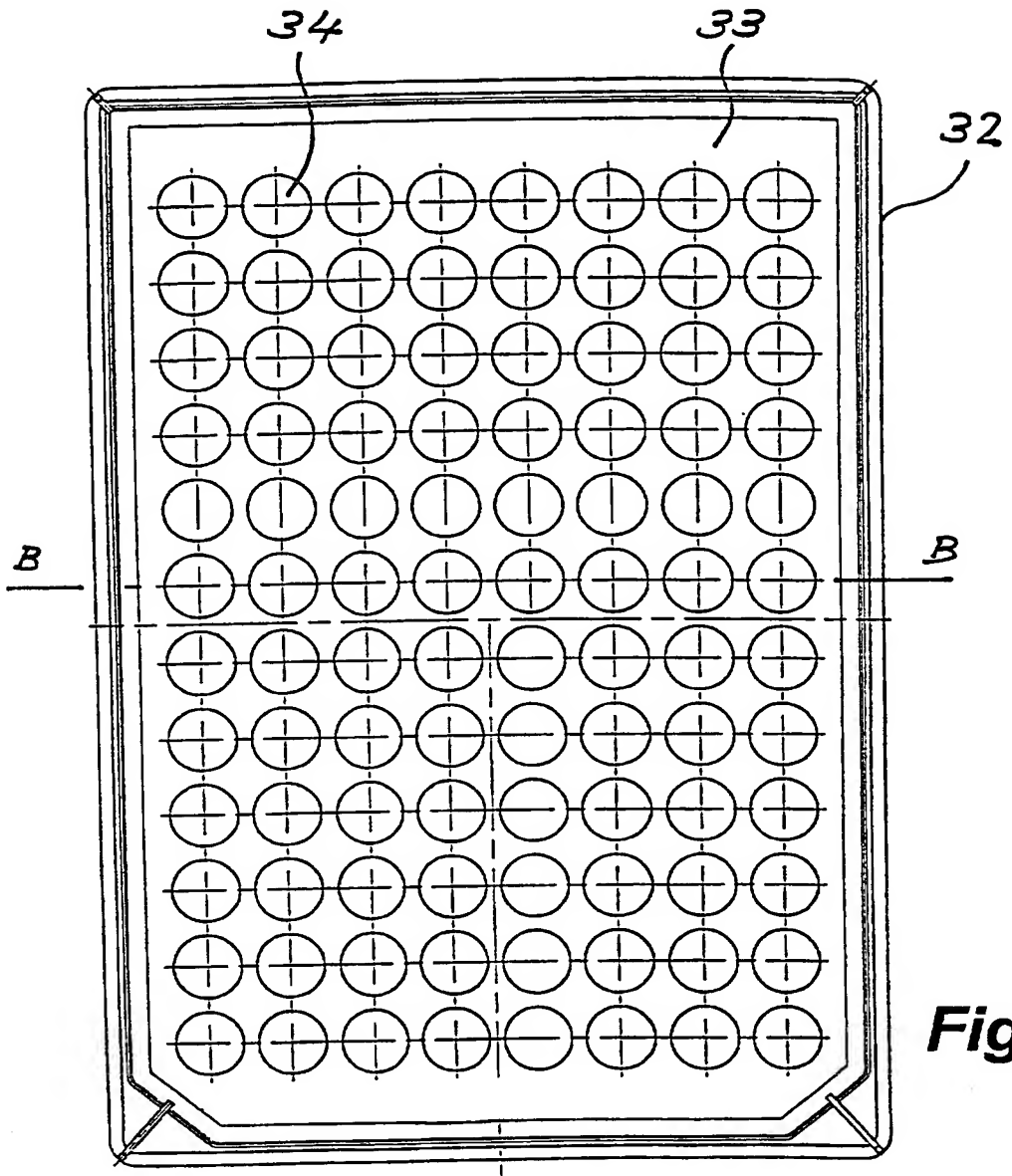


Fig. 5

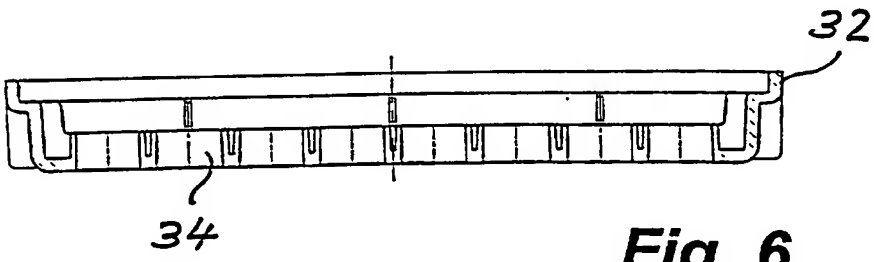
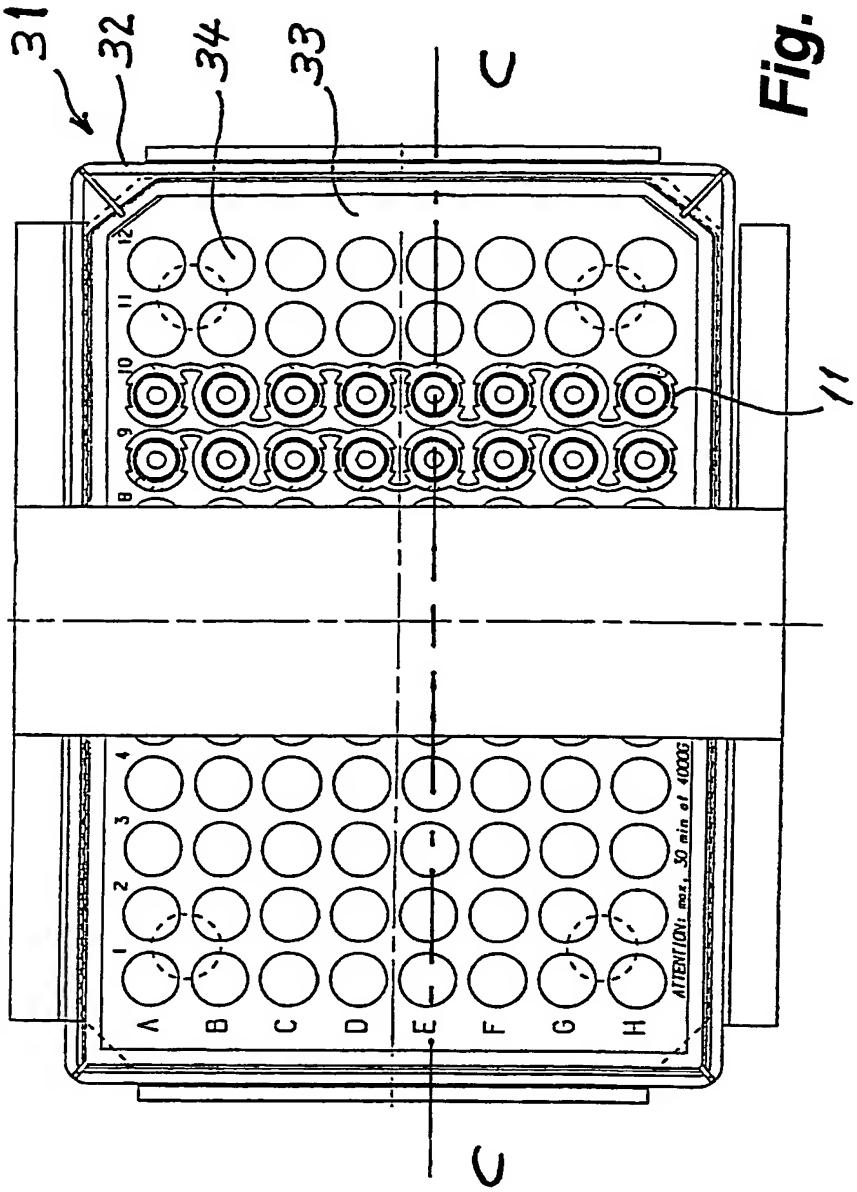


Fig. 6


31
32
34
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ATTENTION: max. 30 min at 4000G
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Fig. 7

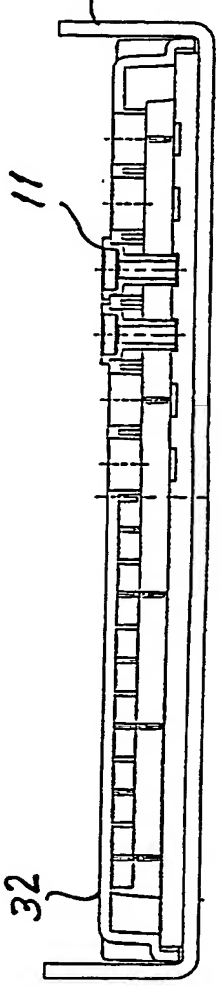
39
11
32

Fig. 8

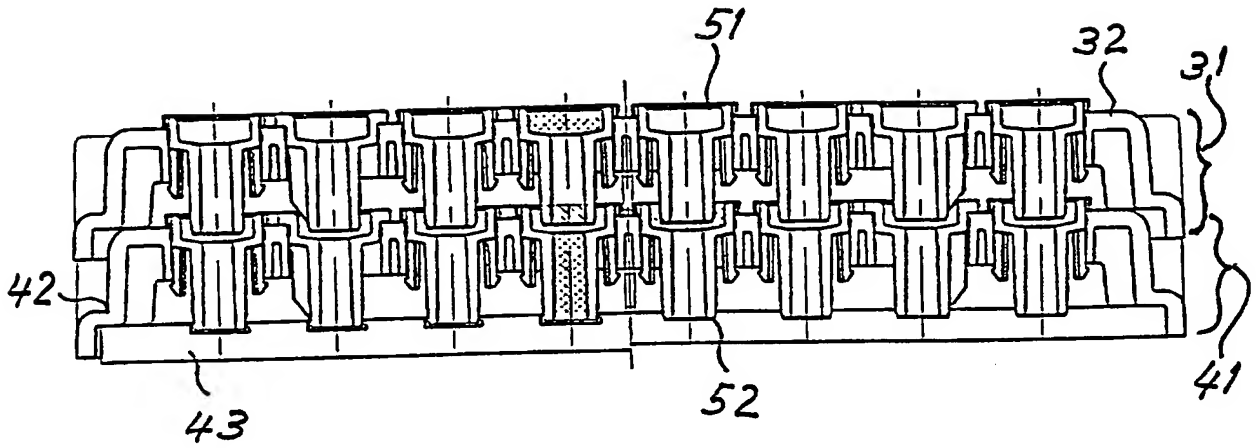

Fig. 9

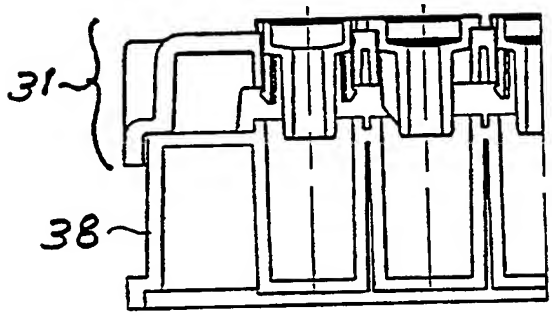

Fig. 10